# EXHIBIT 5

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

**A. 510(k) Number:**

k110035

**B. Purpose for Submission:**

New device (analyzer and reagent)

**C. Measurand:**

Glucose

**D. Type of Test:**

Quantitative Glucose hexokinase (Glucose), photometric

**E. Applicant:**

Thermo Fisher Scientific Oy

**F. Proprietary and Established Names:**

Indiko Clinical Chemistry Analyzer

Indiko Glucose (HK)

**G. Regulatory Information:**

1. Regulation section:

   21 CFR § 862.1345 Glucose test system

   21 CFR § 862.2160 Discrete Photometric Chemistry Analyzer for Clinical Use

2. Classification:

   Class II, I

3. Product code:

   CFR Hexokinase, Glucose

   JJE Analyzer, Chemistry (Photometric, Discrete), For Clinical Use

4. Panel:

   Chemistry 75

**H. Intended Use:**

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Thermo Scientific Indiko Clinical Chemistry Analyzer is a fully automated random access analyzer used to measure a variety of analytes that may be adaptable to the analyzer depending on the reagent used.

   The Indiko Glucose (HK) test system, is intended for *in vitro* diagnostic use in the quantitative determination of the glucose concentration in human plasma on the Indiko analyzer.

   Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma.

3. Special conditions for use statement(s):

   For prescription use.

4. Special instrument requirements:

   Indiko analyzer

**I. Device Description:**

The Indiko is automated random access discrete photometric analyzer, capable of performing up to 30 photometric tests at one time.

Samples are manually loaded onto a sample rack. The sample rack has an integrated barcode reader which allows cup/tube recognition. The barcode reader can read the following codes: code 128, USS Codabar, interleaved 2 of 5 and code 39 with check digit. Non-barcoded samples may also be assayed.

Reaction cells are discrete disposable (single use) multicell cuvettes with 10 reaction measurement cells in a row. There is an on-board capacity of 36 multicell cuvettes (equal to 360 reaction cells), with continuous loading capability, typically 2 hours walk-away time. The quality of the reaction cells is checked at the start of the routine work automatically. The measurements are performed at 37°C.

Reagents are liquid. The reagent bottles are placed on the reagent/sample disk, which holds maximum 30 positions. The reagent/sample disk is refrigerated.

The operating system works with Windows ® XP. The user interface software is graphical. The data input can be done online or by touch screen or mouse or keyboard.

The Glucose (HK) method consists of two reagents. Reagent A (buffer) contains 100 mmol/L Tris buffer (pH7.8) 2.1 mmol/L ATP, 2.1 mmol/L NAD, 4 mmol/L $Mg^{2+}$ and <0.1% $NaN_3$. Reagent B (Enzyme) contains 4 mmol/L $Mg^{2+}$, >7.5 kU/L Hexokinase, >7.5 kU/L G-6-P-DH and <0.1% $NaN_3$. Reagent A is provided in 16 mL bottles and Reagent B in 4 mL bottles.

## J. Substantial Equivalence Information:

1. Predicate device name(s):
   Thermo Fisher DPC T60i Clinical Chemistry Analyzer
   Thermo Fisher DPC T60i Glucose (HK) assay

2. Predicate 510(k) number(s):
   k061107

3. Comparison with predicate:
   The similarities and differences of the analyzer and glucose reagent are summarized below:

| Attribute | Indiko Analyzer | DPC T60i Analyzer |
|---|---|---|
| Indications for use | Is a fully automated random access analyzer used to measure a variety of analytes that may be adaptable to the analyzer depending on the reagent used. | Same |
| Maximum Throughput | 200 tests per hour | 600 tests per hour |
| Methodologies | Photometric | Photometric, Potentiometric |
| Sample Containers Supported | 0.5 ml cups, 2 ml cups, 5 ml tubes (13 x 75 mm), 7 ml tubes (13 * 100 mm), 10 ml tubes (16 x 100 mm) | 0.5 ml cups, 2 ml cups, 5 ml tubes (13 x 75 mm), 7 ml tubes (13 * 100 mm), 10 ml tubes (16 x 100 mm) |

| Attribute | Indiko Analyzer | DPC T60i Analyzer |
|---|---|---|
| STAT Capability | Yes | Yes |
| Sample ID Input | Manual or Barcode | Manual or Barcode |
| Reagent Barcode Reader | Yes | Yes |
| Incubator Positions | 9 positions * 10 cells = 90 cells | 20 positions * 12 cells = 240 cells |
| Load Assay Protocol Information | User Configurable<br>Electronic file transfer<br>Upload for 2D label | User Configurable |
| Calibration | Programmable | Programmable |
| Operator Interface | Touch screen and keyboard | Touch screen and keyboard |
| Test Modes | Sample orientated, STAT | Random, STAT |
| On-Analyzer Sample Capacity | Flexible from 9 up 45 samples | 6 segments * 14 positions/segment = 84 samples |
| **Attribute** | **Glucose (HK) for the Indiko analyzer** | **Glucose (HK) for the T60 analyzer** |
| Indications for use | Used for the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and of pancreatic islet cell carcinoma. | Same |
| Reagent composition | **Reagent A:** Buffer<br>Tris buffer (pH 7.8)100 mmol/L<br>ATP 2.1 mmol/L<br>NAD 2.1 mmol/L<br>$Mg^{2+}$ 4 mmol/L<br>$NaN_3$ < 0.1 %<br>**Reagent B**: Enzyme<br>$Mg^{2+}$ 4 mmol/L<br>Hexokinase > 7.5 kU/L<br>G-6-P-DH > 7.5 kU/L<br>$NaN_3$ < 0.1 % | Same |
| Sample type | Plasma (Li-heparin) | Serum or plasma (Li-heparin) |
| Measuring range | 5 – 720 mg/dL | 5 – 720 mg/dL<br>Extended measuring range after secondary dilution:<br>5 – 2160 mg/dL |

**K. Standard/Guidance Document Referenced (if applicable):**

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline- Second Edition (CLSI EP5-A2)
- Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A)
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition (CLSI EP9-A2)
- Interference Testing in Clinical Chemistry; Approved Guideline, Second Edition (CLSI EP7-A2)

**L. Test Principle:**

Glucose is phosphorylated by ATP, in a reaction catalyzed by hexokinase (HK). The glucose-6-phosphate (G-6-P) formed is oxidated to 6-phosphogluconate (6-PG) by glucose-6-phosphate dehydrogenase (G-6-P-DH). In this same reaction an equimolar amount of NAD is reduced to NADH, with a resulting increase in absorbance at 340 nm. The increased absorbance is directly proportional to the amount of glucose in the sample.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

*a. Precision/Reproducibility:*

A precision study was performed using CLSI document EP5-A2 as guideline. Three levels of commercial control material were evaluated on three Indiko Clinical Chemistry Analyzers using three glucose reagent lots, with two runs per day and two replicates per run over 20 days. The total number of measurements was n = 84. The results are summarized below.

| | Low mean 57 mg/dL | | Middle mean 86 mg/dL | | High mean 269 mg/dL | |
|---|---|---|---|---|---|---|
| | SD | CV% | SD | CV% | SD | CV% |
| Repeatability (Within Run) | 0.6 | 1.0 | 0.5 | 0.6 | 2.0 | 0.8 |
| Between run | 0.3 | 0.6 | 1.0 | 1.1 | 1.6 | 0.6 |
| Within Device (Total) | 1.0 | 1.8 | 1.6 | 1.8 | 4.1 | 1.5 |

A second precision study was performed using lithium heparin samples at three glucose levels. CLSI document EP5-A2 was used as a guideline; however the study was performed for 10 days. Samples were evaluated on one Indiko analyzer, with two runs per day and two replicates per run, with the number of measurements being n = 40. The results are summarized below.

| | Low mean 53 mg/dL | | Middle mean 123 mg/dL | | High mean 203 mg/dL | |
|---|---|---|---|---|---|---|
| | SD | CV% | SD | CV% | SD | CV% |
| Repeatability (Within Run) | 0.3 | 0.7 | 0.7 | 0.6 | 1.7 | 0.8 |
| Between run | 0.4 | 0.8 | 1.5 | 1.2 | 1.3 | 0.6 |
| Within Device (Total) | 0.8 | 1.6 | 1.8 | 1.5 | 3.2 | 1.5 |

*b. Linearity/assay reportable range:*

A linearity study across the claimed assay range 5-720 mg/dL was performed by preparing two plasma samples with very low and high glucose concentrations. The low and high pools were mixed in different proportions to create nine dilutions. Eleven samples in all were assayed in triplicate

Data was analyzed using 1st, 2nd, and 3rd order least square regressions according to CLSI protocol EP6-A. Based on the analysis the sponsor determined that second order regression was the best fit and yielded the following equation:

Second order: $y = -4.075E\text{-}05x^2 + 1.028x - 0.03861$, Std. Error 4.242

Based on these results, the sponsor claims that the assay is linear from 5-720 mg/dL

*c. Traceability, Stability, Expected values (controls, calibrators, or methods):*

The calibrator (sCal) and multi-analyte controls (Nortrol and Abtrol) were previously cleared under k061107.

The expected values and value assignment process were reviewed for this test system. The value sheet for sCal, Nortrol, and Abtrol will specify values for Indiko.

*d. Detection limit:*

A detection limit study was performed using CLSI EP17-A as a guide. The sponsor performed the following studies. Limit of Blank (LoB) was determined by running a blank sample (saline) 96 times total on two Indiko analyzers with two lots of Glucose (HK) reagent. The limit of detection (LoD) and limit of quantitation (LoQ) was determined by assaying 3 low glucose concentration plasma samples on two Indiko analyzers and two reagent lots over two days, for a total of 42 replicates each.

The sponsor states that the LoB represents the highest measurement result that is

likely to be observed for an analyte-free sample. LoB is equal to 0.54 mg/dL. The LoD/LoQ represents the lowest actual concentration in a sample that can be quantitatively determined. The LoD/LoQ is stated to be 0.54 mg/dL

The claimed lower limit of the measuring range is 5 mg/dL. Glucose values <5 mg/dL are flagged "Test limit low" by the analyzer.

e. *Analytical specificity:*
Testing for endogenous interfering substances was based on CLSI EP-7A2. Testing was performed on a minimum of five concentrations for each potential interferant. Plasma samples with three glucose levels, low level 74-77 mg/dl, middle level 109-112 mg/dl and high level 271-278 mg/dl were used in the evaluation. Samples with the interferents were tested and compared to the same sample without the interferent (control).

The sponsor defined non-significant interference as the highest level tested that recovers within ±5% of the control sample.

Based on the studies performed the results support the following claims:

Hemolysis: No interference found up to 1000 mg/dL of hemoglobin.

Bilirubin (conjugated): No interference found up to 47 mg/dL.

Bilirubin (unconjugated): No interference found up to 50 mg/dL.

Lipemia: No interference found up to 1000 mg/dL of Intralipid®.

The labeling refers users to information on other potentially interfering substances (Young, D.S. *Effect of Drugs on Clinical Laboratory Tests, Fifth Edition*, AACC Presss, 2000).

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

A method comparison study was performed using CLSI document EP9-A2 as a guide. One hundred and seventeen (117) lithium plasma samples were analyzed with the Indiko Glucose test system and the DPC T60 glucose test system. Of these samples, 101 were neat lithium plasma. Twelve (12) were spiked to create samples with high glucose and four (4) were diluted to create samples with very low glucose. The results are summarized below.

| | |
|---|---|
| Deming regression | y = 1.005x + 0.677 |
| Slope, 95% Confidence Interval | 1.003 to 1.008 |
| Intercept, 95% Confidence Interval (ng/mL) | 0.197 to 1.157 |
| Correlation Coefficient, r | 1.00 |
| N | 117 |
| Range (ng/mL) | 6-700 |

*b. Matrix comparison:*

The device is intended for lithium heparin plasma only

3. Clinical studies:

*a. Clinical Sensitivity:*

Not applicable

*b. Clinical specificity:*

Not applicable

*c. Other clinical supportive data (when a. and b. are not applicable):*

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Expected values are based on literature. The labeling recommends that each laboratory verify the use of these values with the intended patient population.

Plasma (fasting)
Adults: 60 - 109 mg/dl (3.3. - 6.0 mmol/l)

Jacobs, D.S., DeMott, W.R. and Oxley, D.K., Laboratory Test Handbook 3rd Edition, 2004, LEXI-COMP, INC, Hudson (Cleveland), OH: p. 644

**N. Instrument Name:**

Indiko Clinical Chemistry Analyzer

**O. System Descriptions:**

1. Modes of Operation:
   Benchtop fully automated random access analyzer

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __x_____ or No _____

   The software documentation provided demonstrates the Indiko Analyzer was designed under adequate software lifecycle processes.

3. Specimen Identification:

   Barcode or manual entry

4. Specimen Sampling and Handling:

   Samples can be manually loaded into sample rack for direct sampling from specimen tube or sample cup.

5. Calibration:

   On-board programmable calibration.

6. Quality Control:

   The software contains a quality control program that evaluates control results and determines if they are within specified acceptable limits.

   Analyzer labeling recommends that quality control be performed daily. Users are instructed to follow local, state and federal regulations with regard to the frequency of running quality control.

**P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:**

EMC testing was evaluated and certified by SGS Fimko Ltd. and a letter of attestation was issued to Thermo Fisher on June 2, 2010.

**Q. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**R. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.